

Fig. 9

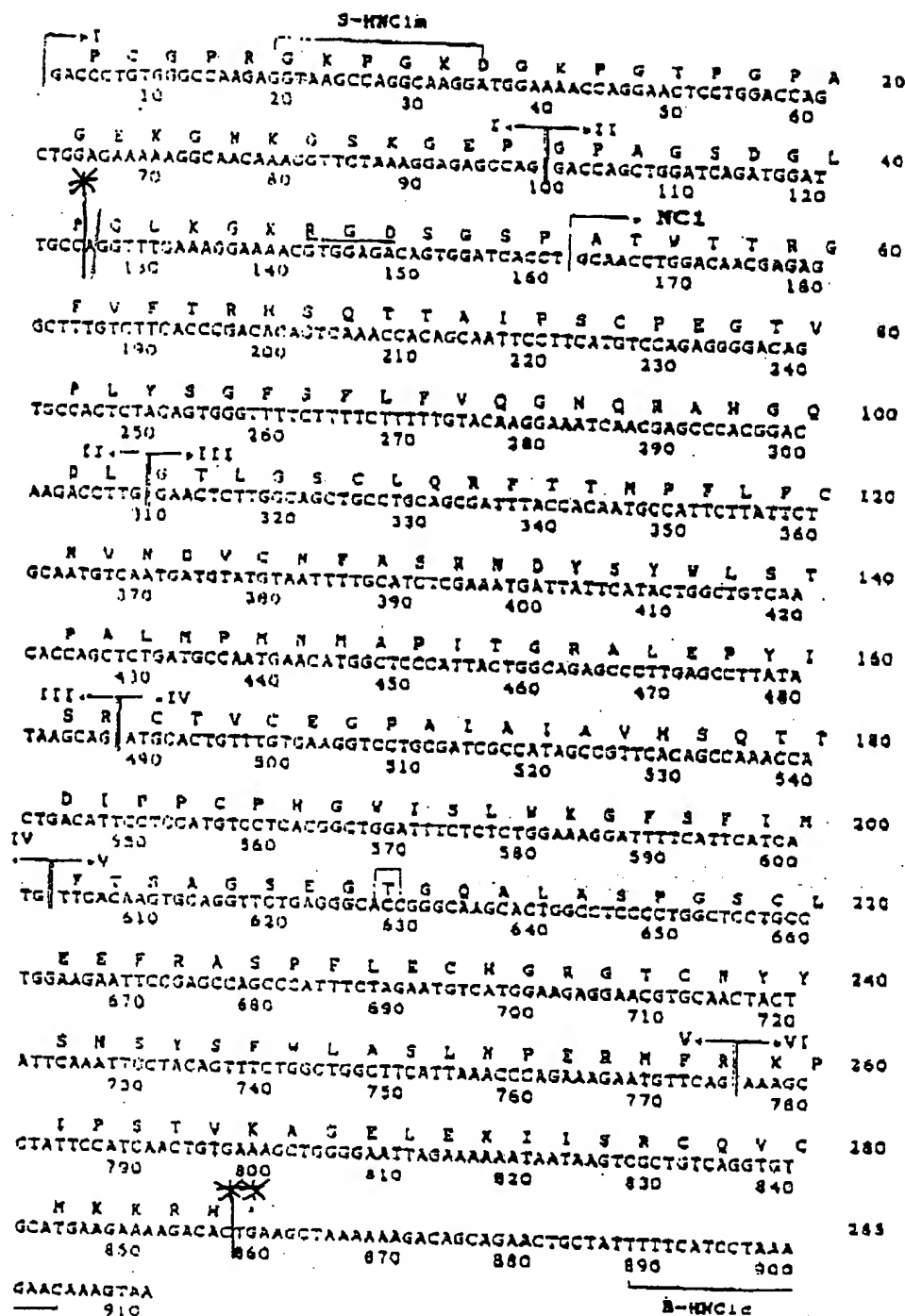


FIG. 2. Nucleotide and derived amino acid sequence of HGA3.3 exons. Bent arrows indicate the 5'- and 3'-borders of each exon and the beginning of the NC1 domain. The RGD sequence is underlined. The boxed amino acid is different from that previously reported (11). Positions of the oligonucleotides S-HNC1m and B-HNC1c used for PCR amplification of a human $\alpha 3$ (IV) cDNA are indicated. Amino Acids 1-67 have not been previously reported (11).

EXHIBIT

A

tled3

ay, June 7, 1998 12:44 PM

```

      10      20      30      40
*      *      *      *
GLK GKR GDS GSP ATW TTR GFV FTR HSQ TTA IPS CPE GTV PLY SGF
____1427 TO 1670 OF FULL LENGTH A3 CHAIN OF TYPE IV____>

      50      60      70      80      90
*      *      *      *      *
SFL FVQ GNQ RAH GQD LGT LGS CLQ RFT TMP FLF CNV NDV CNF ASR
____1427 TO 1670 OF FULL LENGTH A3 CHAIN OF TYPE IV____>

      100     110     120     130
*      *      *      *      *
NDY SYW LST PAL MPM NMA PIT GRA LEP YIS RCT VCE GPA IAI AVH
____1427 TO 1670 OF FULL LENGTH A3 CHAIN OF TYPE IV____>

      140     150     160     170     180
*      *      *      *      *
SQT TDI PPC PHG WIS LWK GFS FIM FTS AGS EGT GQA LAS PGS CLE
____1427 TO 1670 OF FULL LENGTH A3 CHAIN OF TYPE IV____>

      190     200     210     220
*      *      *      *      *
EFR ASP FLE CHG RGT CNY YSN SYS FWL ASL NPE RMF RKP IPS TVK
____1427 TO 1670 OF FULL LENGTH A3 CHAIN OF TYPE IV____>

      230     240
*      *
AGE LEK IIS RCQ VCM KKR H
____1427 TO 1670 OF FU____>

```

Fig. 10

FIG. 18A

pET22b(+) forward primer:

5'-CGGGAT CCA GGT TTG AAA GGA AAA CGT-3' (SEQ ID NO:11)

pET22b(+) reverse primer:

5'-CCCAAGCTT TCA GTG TCT TTT CTT CAT-3' (SEQ ID NO:12)

5	10	15	20	25	30	35	40	45
cca ggt ttg aaa gga aaa cgt	gga gac agt	gga tca cct	gca acc					
50	55	60	65	70	75	80	85	90
tgg aca acg	aga ggc ttt	gtc ttc acc	cga cac agt	caa acc	aca			
95	100	105	110	115	120	125	130	135
gca att cct	tca tgt cca	gag ggg aca	gtg cca ctc	tac agt	ggg			
140	145	150	155	160	165	170	175	180
ttt tct ttt	ctt ttt gta	caa gga aat	caa cga gcc	cac gga	caa			
185	190	195	200	205	210	215	220	225
gac ctt gga	act ctt ggc	agc tgc ctg	cag cga ttt	acc aca	atg			
230	235	240	245	250	255	260	265	270
cca ttc tta	ttc tgc aat	gtc aat gat	gta tgt aat	ttt gca	tct			
275	280	285	290	295	300	305	310	315
cga aat gat	tat tca tac	tgg ctg tca	aca cca gct	ctg atg	cca			
320	325	330	335	340	345	350	355	360
atg aac atg	gct ccc att	act ggc aga	gcc ctt gag	cct tat	ata			
365	370	375	380	385	390	395	400	405
agc aga tgc	act gtt tgt	gaa ggt cct	gcg atc gcc	ata gcc	gtt			
410	415	420	425	430	435	440	445	450
cac agc caa	acc act gac	att cct cca	tgt cct cac	ggc tgg	att			
455	460	465	470	475	480	485	490	495
tct ctc tgg	aaa gga ttt	tca ttc atc	atg ttc aca	agt gca	ggt			
500	505	510	515	520	525	530	535	540
tct gag ggc	acc ggg caa	gca ctg gcc	tcc cct ggc	tcc tgc	ctg			
545	550	555	560	565	570	575	580	585
gaa gaa ttc	cga gcc agc	cca ttt cta	gaa tgt cat	gga aga	gga			
590	595	600	605	610	615	620	625	630
acg tgc aac	tac tat tca	aat tcc tac	agt ttc tgg	ctg gct	tca			
635	640	645	650	655	660	665	670	675
tta aac cca	gaa aga atg	ttc aga aag	cct att cca	tca act	gtg			
680	685	690	695	700	705	710	715	720
aaa gct ggg	gaa tta gaa	aaa ata ata	agt cgc	tgt cag	gtg tgc			
725	730	735						
<u>atg aag aaa aga cac tga</u>			(SEQ ID NO:9)					

pET22b-α3(IV) NC1 = nucleotides 4 through 732

Tumstatin 333 = nucleotides 4 through 772

Tumstatin 334 - nucleotide 376 through 732

373



FIG. 18B

*
 5 10 15 20 25 30 35 40 45
 XGL KGK RGD SGS PAT WTT RGF VFT RHS QTT AIP SCP EGT VPL YSG
 50 55 60 65 70 75 80 85 90
 FSF LFV QGN QRA HGQ DLG TLG SCL QRF TTM PFL FCN VND VCN FAS
 95 100 105 110 115 120 125 130 135
 RND YSY WLS TPA LMP MNM API TGR ALE PYI SRC TVC EGP AIA IAV
 140 145 150 155 160 165 170 175 180
 HSQ TTD IPP CPH GWI SLW KGF SFI MFT SAG SEG TGQ ALA SPG SCL
 185 190 195 200 205 210 215 220 225
 EEF RAS PFL ECH GRG TCN YYS NSY SFW LAS LNP ERM FRK PIP STV
 230 235 240 245-244
 KAG ELE KII SRC QVC MKK RH (SEQ ID NO:10)

pET22b α 3(IV) NC1 = residues 1 through 245-244
 Tumstatin 333 = residues 1 through 125-124
 Tumstatin 334 = residues 126 through 245-244
 125



FIG. 42

T1 GP-A
PGLKGKRGDSGSPATWTTTRGFVFTRHSQTTAIPSCPEGTVPLY

T2 T3 T4
SGFSFLFVQGNQRAHGQDLGTLGSC LQRFTTMPFLFCNVNDVC

T3 T5
T4 T6
NFASRNDYSYWLSTPALMPMNMAPITGRALEPYISRCTVCEGP

T6 GP-B
AIAIAVHSQTTDIPPCPHGWISLWKGFSFIMFTSAGSEGTGQA
LASPGSCLEEFRA SPFLECHGRGTCNYYSNSYSFWLASLNPER
MFRKPI PSTVKAGELEKII SRCQVCMKKRH



SEQUENCE LISTING

<110> Raghuram Kalluri

<120> ANTI-ANGIOGENIC PROTEINS AND FRAGMENTS
AND METHODS OF USE THEREOF

<130> 1440.1027-016

{ <140> US 10/032,221
 { <141> 2001-12-21

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<151> 2001-01-08

<150> US 09/543,371

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gac cca cag tgt cct tct ggg acc aaa att ctt tac cac ggg tac tct
 Asp Pro Gln Cys Pro Ser Gly Thr Lys Ile Leu Tyr His Gly Tyr Ser
 20 25 30

96

ttg ctc tac gtg caa ggc aat gaa cgg gcc cat gga cag gac ttg ggc
 Leu Leu Tyr Val Gln Gly Asn Glu Arg Ala His Gly Gln Asp Leu Gly
 35 40 45

144

EXHIBIT

E

tabbles

2/21

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Thr Ala Gly Ser Cys Leu Arg Lys Phe Ser Thr Met Pro Phe Leu Phe	
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tgc aat att aac aac gtg tgc aac ttt gca tca cga aat gac tac tcg	240
Cys Asn Ile Asn Asn Val Cys Asn Phe Ala Ser Arg Asn Asp Tyr Ser	
65 70 75 80	
tac tgg ctg tcc acc cct gag ccc atg ccc atg tca atg gca ccc atc	288
Tyr Trp Leu Ser Thr Pro Glu Pro Met Pro Met Ser Met Ala Pro Ile	
85 90 95	
acg ggg gaa aac ata aga cca ttt att agt agg tgt gct gtg tgt gag	336
Thr Gly Glu Asn Ile Arg Pro Phe Ile Ser Arg Cys Ala Val Cys Glu	
100 105 110	
gcg cct gcc atg gtg atg gcc gtg cac agc cag acc att cag atc cca	384
Ala Pro Ala Met Val Met Ala Val His Ser Gln Thr Ile Gln Ile Pro	
115 120 125	
ccg tgc ccc agc ggg tgg tcc tcg ctg tgg atc ggc tac tct ttt gtg	432
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130 135 140	
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145 150 155 160	
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165 170 175	
cac ggc cgt ggg acc tgc aat tac tac gca aac gct tac agc ttt tgg	576
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180 185 190	
ctc gcc acc ata gag agg agc gag atg ttc aag aag cct acg ccg tcc	624
Leu Ala Thr Ile Glu Arg Ser Glu Met Phe Lys Lys Pro Thr Pro Ser	
195 200 205	
acc ttg aag gca ggg gag ctg cgc acg cac gtc agc cgc tgc caa gtc	672
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20 25 30	

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  50          55          60
Cys Asn Ile Asn Asn Val Cys Asn Phe Ala Ser Arg Asn Asp Tyr Ser
  65          70          75          80
Tyr Trp Leu Ser Thr Pro Glu Pro Met Pro Met Ser Met Ala Pro Ile
          85          90          95
Thr Gly Glu Asn Ile Arg Pro Phe Ile Ser Arg Cys Ala Val Cys Glu
          100          105          110
Ala Pro Ala Met Val Met Ala Val His Ser Gln Thr Ile Gln Ile Pro
          115          120          125
Pro Cys Pro Ser Gly Trp Ser Ser Leu Trp Ile Gly Tyr Ser Phe Val
          130          135          140
Met His Thr Ser Ala Gly Ala Glu Gly Ser Gly Gln Ala Leu Ala Ser
          145          150          155          160
Pro Gly Ser Cys Leu Glu Glu Phe Arg Ser Ala Pro Phe Ile Glu Cys
          165          170          175
His Gly Arg Gly Thr Cys Asn Tyr Tyr Ala Asn Ala Tyr Ser Phe Trp
          180          185          190
Leu Ala Thr Ile Glu Arg Ser Glu Met Phe Lys Lys Pro Thr Pro Ser
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Thr Leu Lys Ala Gly Glu Leu Arg Thr His Val Ser Arg Cys Gln Val
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Arresten

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Arresten

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4/21

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ctg tac ttc gag ggc cag gag aag gcg cac aac cag gac ctg ggg ctg Leu Tyr Phe Glu Gly Gln Glu Lys Ala His Asn Gln Asp Leu Gly Leu 35 40 45	144
gcg ggc tcc tgc ctg gcg cgg ttc agc acc atg ccc ttc ctg tac tgc Ala Gly Ser Cys Leu Ala Arg Phe Ser Thr Met Pro Phe Leu Tyr Cys 50 55 60	192
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atc gcc atc gcg gtc cac agt cag gat gtc tcc atc cca cac tgc cca Ile Ala Ile Ala Val His Ser Gln Asp Val Ser Ile Pro His Cys Pro 115 120 125	384
gct ggg tgg ccg agt ttg tgg atc gga tat tcc ttc ctc atg cac acg Ala Gly Trp Arg Ser Leu Trp Ile Gly Tyr Ser Phe Leu Met His Thr 130 135 140	432
gcg gcg gga gac gaa ggc ggt ggc caa tca ctg gtg tca ccg ggc agc Ala Ala Gly Asp Glu Gly Gly Gly Gln Ser Leu Val Ser Pro Gly Ser 145 150 155 160	480
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cgc ggc acc tgc cac tac tac gcc aac aag tac agc ttc tgg ctg acc Arg Gly Thr Cys His Tyr Tyr Ala Asn Lys Tyr Ser Phe Trp Leu Thr 180 185 190	576
acc att ccc gag cag agc ttc cag ggc tcg ccc tcc gcc gac acg ctc Thr Ile Pro Glu Gln Ser Phe Gln Gly Ser Pro Ser Ala Asp Thr Leu 195 200 205	624
aag gcc ggc ctc atc cgc aca cac atc agc cgc tgc cag gtg tgc atg Lys Ala Gly Leu Ile Arg Thr His Ile Ser Arg Cys Gln Val Cys Met 210 215 220	672
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 35 40 45
 Ala Gly Ser Cys Leu Ala Arg Phe Ser Thr Met Pro Phe Leu Tyr Cys
 50 55 60
 Asn Pro Gly Asp Val Cys Tyr Tyr Ala Ser Arg Asn Asp Lys Ser Tyr
 65 70 75 80
 Trp Leu Ser Thr Thr Ala Pro Leu Pro Met Met Pro Val Ala Glu Asp
 85 90 95
 Glu Ile Lys Pro Tyr Ile Ser Arg Cys Ser Val Cys Glu Ala Pro Ala
 100 105 110
 Ile Ala Ile Ala Val His Ser Gln Asp Val Ser Ile Pro His Cys Pro
 115 120 125
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 130 135 140
 Ala Ala Gly Asp Glu Gly Gly Gly Gln Ser Leu Val Ser Pro Gly Ser
 145 150 155 160
 Cys Leu Glu Asp Phe Arg Ala Thr Pro Phe Ile Glu Cys Asn Gly Gly
 165 170 175
 Arg Gly Thr Cys His Tyr Tyr Ala Asn Lys Tyr Ser Phe Trp Leu Thr
 180 185 190
 Thr Ile Pro Glu Gln Ser Phe Gln Gly Ser Pro Ser Ala Asp Thr Leu
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 Lys Asn Leu
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Thr Thr Arg Gly Phe Val Phe Thr Arg His Ser Gln Thr Thr Ala Ile
20 25 30

cct tca tgt cca gag ggg aca gtg cca ctc tac agt ggg ttt tct ttt 144
Pro Ser Cys Pro Glu Gly Thr Val Pro Leu Tyr Ser Gly Phe Ser Phe
35 40 45

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50 55 60

ctt ggc agc tgc ctg cag cga ttt acc aca atg cca ttc tta ttc tgc 240
Leu Gly Ser Cys Leu Gln Arg Phe Thr Thr Met Pro Phe Leu Phe Cys
65 70 75 80

aat gtc aat gat gta tgt aat ttt gca tct cga aat gat tat tca tac 288
Asn Val Asn Asp Val Cys Asn Phe Ala Ser Arg Asn Asp Tyr Ser Tyr
85 90 95

tgg ctg tca aca cca gct ctg atg cca atg aac atg gct ccc att act 336
Trp Leu Ser Thr Pro Ala Leu Met Pro Met Asn Met Ala Pro Ile Thr
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Gly Arg Ala Leu Glu Pro Tyr Ile Ser Arg Cys Thr Val Cys Glu Gly
115 120 125

cct gcg atc gcc ata gcc gtt cac agc caa acc act gac att cct cca 432
Pro Ala Ile Ala Ile Ala Val His Ser Gln Thr Thr Asp Ile Pro Pro
130 135 140

tgt cct cac ggc tgg att tct ctc tgg aaa gga ttt tca ttc atc atg 480
Cys Pro His Gly Trp Ile Ser Leu Trp Lys Gly Phe Ser Phe Ile Met
145 150 155 160

ttc aca agt gca ggt tct gag ggc acc ggg caa gca ctg gcc tcc cct 528
Phe Thr Ser Ala Gly Ser Glu Gly Thr Gly Gln Ala Leu Ala Ser Pro
165 170 175

ggc tcc tgc ctg gaa gaa ttc cga gcc agc cca ttt cta gaa tgt cat 576
Gly Ser Cys Leu Glu Glu Phe Arg Ala Ser Pro Phe Leu Glu Cys His

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180										185					190					
gga	aga	gga	acg	tgc	aac	tac	tat	tca	aat	tcc	tac	agt	ttc	tgg	ctg	624				
Gly	Arg	Gly	Thr	Cys	Asn	Tyr	Tyr	Ser	Asn	Ser	Tyr	Ser	Phe	Trp	Leu					
		195					200					205								
gct	tca	tta	aac	cca	gaa	aga	atg	ttc	aga	aag	cct	att	cca	tca	act	672				
Ala	Ser	Leu	Asn	Pro	Glu	Arg	Met	Phe	Arg	Lys	Pro	Ile	Pro	Ser	Thr					
	210					215					220									
gtg	aaa	gct	ggg	gaa	tta	gaa	aaa	ata	ata	agt	cgc	tgt	cag	gtg	tgc	720				
Val	Lys	Ala	Gly	Glu	Leu	Glu	Lys	Ile	Ile	Ser	Arg	Cys	Gln	Val	Cys					
225					230					235					240					
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Met	Lys	Lys	Arg	His																
				245																

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8/21

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Arresten

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Canstatin

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50 55 60
Leu Gly Ser Cys Leu Gln Arg Phe Thr Thr Met Pro Phe Leu Phe Cys
65 70 75 80
Asn Val Asn Asp Val Cys Asn Phe Ala Ser Arg Asn Asp Tyr Ser Tyr
85 90 95
Trp Leu Ser Thr Pro Ala Leu Met Pro Met Asn Met Ala Pro Ile Thr
100 105 110
Gly Arg Ala Leu Glu Pro Tyr Ile Ser Arg Cys Thr Val Cys Glu Gly~~

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Cys Pro His Gly Trp Ile Ser Leu Trp Lys Gly Phe Ser Phe Ile Met
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Phe Thr Ser Ala Gly Ser Glu Gly Thr Gly Gln Ala Leu Ala Ser Pro
165 170 175
Gly Ser Cys Leu Glu Glu Phe Arg Ala Ser Pro Phe Leu Glu Cys His
180 185 190
Gly Arg Gly Thr Cys Asn Tyr Tyr Ser Asn Ser Tyr Ser Phe Trp Leu
195 200 205
Ala Ser Leu Asn Pro Glu Arg Met Phe Arg Lys Pro Ile Pro Ser Thr
210 215 220
Val Lys Ala Gly Glu Leu Glu Lys Ile Ile Ser Arg Cys Gln Val Cys
225 230 235 240
~~Met Lys Lys Arg~~

<210> 20
<211> 124
<212> PRT
<213> Artificial Sequence

<220>
<223> Tumstatin 333 (amino acids ~~1-125~~ ¹⁻¹²⁴ of SEQ ID NO:10)

<400> 20
Gly Leu Lys Gly Lys Arg Gly Asp Ser Gly Ser Pro Ala Thr Trp Thr
1 5 10 15
Thr Arg Gly Phe Val Phe Thr Arg His Ser Gln Thr Thr Ala Ile Pro
20 25 30
Ser Cys Pro Glu Gly Thr Val Pro Leu Tyr Ser Gly Phe Ser Phe Leu
35 40 45
Phe Val Gln Gly Asn Gln Arg Ala His Gly Gln Asp Leu Gly Thr Leu
50 55 60
Gly Ser Cys Leu Gln Arg Phe Thr Thr Met Pro Phe Leu Phe Cys Asn
65 70 75 80
Val Asn Asp Val Cys Asn Phe Ala Ser Arg Asn Asp Tyr Ser Tyr Trp
85 90 95
Leu Ser Thr Pro Ala Leu Met Pro Met Asn Met Ala Pro Ile Thr Gly
100 105 110
Arg Ala Leu Glu Pro Tyr Ile Ser Arg Cys Thr Val
115 120

<210> 21
<211> ~~119~~ ¹²⁰
<212> PRT
<213> Artificial Sequence

<220>
<223> Tumstatin 334 (amino acids ~~126-244~~ ¹²⁵ of SEQ ID NO:10)

<400> 21
Cys Glu Gly Pro Ala Ile Ala Ile Ala Val His Ser Gln Thr Thr Asp
1 5 10 15
Ile Pro Pro Cys Pro His Gly Trp Ile Ser Leu Trp Lys Gly Phe Ser

```
<210> 22
<211> 191
<212> PRT
<213> Artificial Sequence
```

<div> <div><400> 22</div> <div> <div>Asn</div> <div>Gln</div> <div>Arg</div> <div>Ala</div> <div>His</div> <div>Gly</div> <div>Gln</div> <div>Asp</div> <div>Leu</div> <div>Gly</div> <div>Thr</div> <div>Leu</div> <div>Gly</div> <div>Ser</div> <div>Cys</div> <div>Leu</div> </div> </div>																	
1				5					10				15				
	Gln	Arg	Phe	Thr	Thr	Met	Pro	Phe	Leu	Phe	Cys	Asn	Val	Asn	Asp	Val	
			20					25					30				
	Cys	Asn	Phe	Ala	Ser	Arg	Asn	Asp	Tyr	Ser	Tyr	Trp	Leu	Ser	Thr	Pro	
		35						40				45					
	Ala	Leu	Met	Pro	Met	Asn	Met	Ala	Pro	Ile	Thr	Gly	Arg	Ala	Leu	Glu	
	50						55					60					
	Pro	Tyr	Ile	Ser	Arg	Cys	Thr	Val	Cys	Glu	Gly	Pro	Ala	Ile	Ala	Ile	
65						70					75					80	
	Ala	Val	His	Ser	Gln	Thr	Thr	Asp	Ile	Pro	Pro	Cys	Pro	His	Gly	Trp	
				85					90					95			
	Ile	Ser	Leu	Trp	Lys	Gly	Phe	Ser	Phe	Ile	Met	Phe	Thr	Ser	Ala	Gly	
			100						105					110			
	Ser	Glu	Gly	Thr	Gly	Gln	Ala	Leu	Ala	Ser	Pro	Gly	Ser	Cys	Leu	Glu	
		115						120					125				
	Glu	Phe	Arg	Ala	Ser	Pro	Phe	Leu	Glu	Cys	His	Gly	Arg	Gly	Thr	Cys	
		130					135					140					
	Asn	Tyr	Tyr	Ser	Asn	Ser	Tyr	Ser	Phe	Trp	Leu	Ala	Ser	Leu	Asn	Pro	
145						150					155					160	
	Glu	Arg	Met	Phe	Arg	Lys	Pro	Ile	Pro	Ser	Thr	Val	Lys	Ala	Gly	Glu	
				165						170					175		
	Leu	Glu	Lys	Ile	Ile	Ser	Arg	Cys	Gln	Val	Cys	Met	Lys	Lys	Arg	His	
			180						185					190			

<220>
<223> Tum-2 (amino acids 1-132 of SEQ ID NO:10)

12/21

<400> 23

~~Pro~~ Gly Leu Lys Gly Lys Arg Gly Asp Ser Gly Ser Pro Ala Thr Trp
1 5 10 15
Thr Thr Arg Gly Phe Val Phe Thr Arg His Ser Gln Thr Thr Ala Ile
20 25 30
Pro Ser Cys Pro Glu Gly Thr Val Pro Leu Tyr Ser Gly Phe Ser Phe
35 40 45
Leu Phe Val Gln Gly Asn Gln Arg Ala His Gly Gln Asp Leu Gly Thr
50 55 60
Leu Gly Ser Cys Leu Gln Arg Phe Thr Thr Met Pro Phe Leu Phe Cys
65 70 75 80
Asn Val Asn Asp Val Cys Asn Phe Ala Ser Arg Asn Asp Tyr Ser Tyr
85 90 95
Trp Leu Ser Thr Pro Ala Leu Met Pro Met Asn Met Ala Pro Ile Thr
100 105 110
Gly Arg Ala Leu Glu Pro Tyr Ile Ser Arg Cys Thr Val Cys Glu Gly
115 120 125
Pro Ala Ile Ala *Ile*
130

<210> 24

<211> 112

<212> PRT

<213> Artificial Sequence

<220>

<223> Tum-3 (amino acids 133-244 of SEQ ID NO:10)

<400> 24

~~Ile~~ Ala Val His Ser Gln Thr Thr Asp Ile Pro Pro Cys Pro His Gly
1 5 10 15
Trp Ile Ser Leu Trp Lys Gly Phe Ser Phe Ile Met Phe Thr Ser Ala
20 25 30
Gly Ser Glu Gly Thr Gly Gln Ala Leu Ala Ser Pro Gly Ser Cys Leu
35 40 45
Glu Glu Phe Arg Ala Ser Pro Phe Leu Glu Cys His Gly Arg Gly Thr
50 55 60
Cys Asn Tyr Tyr Ser Asn Ser Tyr Ser Phe Trp Leu Ala Ser Leu Asn
65 70 75 80
Pro Glu Arg Met Phe Arg Lys Pro Ile Pro Ser Thr Val Lys Ala Gly
85 90 95
Glu Leu Glu Lys Ile Ile Ser Arg Cys Gln Val Cys Met Lys Lys Arg *His*
100 105 110

<210> 25

<211> 64

<212> PRT

<213> Artificial Sequence

<220>

<223> Tum-4 (amino acids 181-244 of SEQ ID NO:10)

<400> 25

~~Glu~~ Glu Phe Arg Ala Ser Pro Phe Leu Glu Cys His Gly Arg Gly Thr
1 5 10 15
Cys Asn Tyr Tyr Ser Asn Ser Tyr Ser Phe Trp Leu Ala Ser Leu Asn
20 25 30

13/21

Pro Glu Arg Met Phe Arg Lys Pro Ile Pro Ser Thr Val Lys Ala Gly
35 40 45
Glu Leu Glu Lys Ile Ile Ser Arg Cys Gln Val Cys Met Lys Lys Arg His
50 55 60

<210> 26
<211> 79
<212> PRT
<213> Artificial Sequence

<220>
<223> Tum-5 (amino acids 54-132 of SEQ ID NO:10)

<400> 26
~~Asn~~ Gln Arg Ala His Gly Gln Asp Leu Gly Thr Leu Gly Ser Cys Leu
1 5 10 15
Gln Arg Phe Thr Thr Met Pro Phe Leu Phe Cys Asn Val Asn Asp Val
20 25 30
Cys Asn Phe Ala Ser Arg Asn Asp Tyr Ser Tyr Trp Leu Ser Thr Pro
35 40 45
Ala Leu Met Pro Met Asn Met Ala Pro Ile Thr Gly Arg Ala Leu Glu
50 55 60
Pro Tyr Ile Ser Arg Cys Thr Val Cys Glu Gly Pro Ala Ile Ala Ile
65 70 75

<210> 27
<211> ~~20~~ 19
<212> PRT
<213> Artificial Sequence

<220>
<223> T1 (amino acids 1-~~20~~ 19 of SEQ ID NO:10)

<400> 27
~~Pro~~ Gly Leu Lys Gly Lys Arg Gly Asp Ser Gly Ser Pro Ala Thr Trp
1 5 10 15
Thr Thr Arg Gly
20

<210> 28
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> T2 (amino acids ~~54-73~~ 53-72 of SEQ ID NO:10)

<400> 28
Asn Gln Arg Ala His Gly Gln Asp Leu Gly Thr Leu Gly Ser Cys Leu
1 5 10 15
Gln Arg Phe Thr
20

<210> 29
<211> 20

14/21

<212> PRT

<213> Artificial Sequence

<220>

<223> T3 (amino acids ~~69-86~~⁶⁸⁻⁸⁷ of SEQ ID NO:10)

<400> 29

Leu	Gln	Arg	Phe	Thr	Thr	Met	Pro	Phe	Leu	Phe	Cys	Asn	Val	Asn	Asp
1				5					10					15	
Val	Cys	Asn	Phe												
				20											

<210> 30

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> T4 (amino acids ~~84-103~~⁸³⁻¹⁰² of SEQ ID NO:10)

<400> 30

Asp	Val	Cys	Asn	Phe	Ala	Ser	Arg	Asn	Asp	Tyr	Ser	Tyr	Trp	Leu	Ser
1				5					10					15	
Thr	Pro	Ala	Leu												
				20											

<210> 31

<211> 19

<212> PRT

<213> Artificial Sequence

<220>

<223> T5 (amino acids ~~99-117~~⁹⁸⁻¹¹⁶ of SEQ ID NO:10)

<400> 31

Ser	Thr	Pro	Ala	Leu	Met	Pro	Met	Asn	Met	Ala	Pro	Ile	Thr	Gly	Arg
1				5					10					15	
Ala	Leu	Glu													

<210> 32

<211> 19

<212> PRT

<213> Artificial Sequence

<220>

<223> T6 (amino acids ~~114-132~~¹¹³⁻¹³¹ of SEQ ID NO:10)

<400> 32

Arg	Ala	Leu	Glu	Pro	Tyr	Ile	Ser	Arg	Cys	Thr	Val	Cys	Glu	Gly	Pro
1				5					10					15	
Ala	Ile	Ala													

<210> 33

15/21

<211> 88
<212> PRT
<213> Artificial Sequence

<220>
<223> Tumstatin-45-132 (amino acids 45-132 of SEQ ID
NO:10)

<400> 33
~~Gly~~ Phe Ser Phe Leu Phe Val Gln Gly Asn Gln Arg Ala His Gly Gln
1 5 10 15
Asp Leu Gly Thr Leu Gly Ser Cys Leu Gln Arg Phe Thr Thr Met Pro
20 25 30
Phe Leu Phe Cys Asn Val Asn Asp Val Cys Asn Phe Ala Ser Arg Asn
35 40 45
Asp Tyr Ser Tyr Trp Leu Ser Thr Pro Ala Leu Met Pro Met Asn Met
50 55 60
Ala Pro Ile Thr Gly Arg Ala Leu Glu Pro Tyr Ile Ser Arg Cys Thr
65 70 75 80
Val Cys Glu Gly Pro Ala Ile Ala *Ile*
85

<210> 34
<211> 88
<212> PRT
<213> Artificial Sequence

<220>
<223> Tumstatin-5-¹²⁵126-C-A (amino acids 45-132 of SEQ ID
NO:10; alanine has been substituted for the
cysteine residue at position 126 of the
full-length Tumstatin molecule) ⁴⁵

<400> 34
~~Gly~~ Phe Ser Phe Leu Phe Val Gln Gly Asn Gln Arg Ala His Gly Gln
1 5 10 15
Asp Leu Gly Thr Leu Gly Ser Cys Leu Gln Arg Phe Thr Thr Met Pro
20 25 30
Phe Leu Phe Cys Asn Val Asn Asp Val Cys Asn Phe Ala Ser Arg Asn
35 40 45
Asp Tyr Ser Tyr Trp Leu Ser Thr Pro Ala Leu Met Pro Met Asn Met
50 55 60
Ala Pro Ile Thr Gly Arg Ala Leu Glu Pro Tyr Ile Ser Arg Cys Thr
65 70 75 80
Val Ala Glu Gly Pro Ala Ile Ala *Ile*
85

<210> 35
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> synthetic blocking peptide

<400> 35
Cys Asp Cys Arg Gly Asp Cys Phe Cys

1

5

<210> 36
 <211> 5
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> synthetic blocking peptide

<400> 36
 Cys Asn Gly Arg Cys
 1 5

<210> 37
 <211> 25
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> T7 (amino acids ^{73 97}~~74-98~~ of SEQ ID NO:10)

<400> 37
 Thr Met Pro Phe Leu Phe Cys Asn Val Asn Asp Val Cys Asn Phe Ala
 1 5 10 15
 Ser Arg Asn Asp Tyr Ser Tyr Trp Leu
 20 25

<210> 38
 <211> 25
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> T7-mutant (amino acids ^{73 97}~~74-98~~ of SEQ ID NO:10;
 methionine has been substituted for the leucine
 residue at position ~~78~~ of the full-length
 Tumstatin molecule, and isoleucine has been
 substituted for valine at position ~~81~~, and
 asparagine has been substituted for aspartic acid
 at position ~~84~~
⁸³)

<400> 38
 Thr Met Pro Phe Met Phe Cys Asn Ile Asn Asn Val Cys Asn Phe Ala
 1 5 10 15
 Ser Arg Asn Asp Tyr Ser Tyr Trp Leu
 20 25

<210> 39
 <211> 27
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> T8 (amino acids ^{968 94}~~69-95~~ of SEQ ID NO:10; lysine has

17/21

been substituted for the leucine residue at
position ~~68~~ of the full-length Tumstatin molecule)

<400> 39

Lys Gln Arg Phe Thr Thr Met Pro Phe Leu Phe Cys Asn Val Asn Asp
1 5 10 15
Val Cys Asn Phe Ala Ser Arg Asn Asp Tyr Ser
20 25

<210> 40

<211> 27

<212> PRT

<213> Artificial Sequence

<220>

<223> T8-3 (amino acids ~~68-95~~^{68 94} of SEQ ID NO:10; lysine
has been substituted for the leucine residue at
position ~~68~~ of the full-length Tumstatin molecule,
and serine has been substituted for the cysteine
residues at positions ~~80~~ and ~~85~~^{79 85})

<400> 40

Lys Gln Arg Phe Thr Thr Met Pro Phe Leu Phe Ser Asn Val Asn Asp
1 5 10 15
Val Ser Asn Phe Ala Ser Arg Asn Asp Tyr Ser
20 25

<210> 41

<211> 19

<212> PRT

<213> Artificial Sequence

<220>

<223> TP3 (amino acids ~~77-95~~^{76 94} of SEQ ID NO:10; lysine has
been substituted for the phenylalanine residue at
position ~~77~~ of the full-length Tumstatin molecule,
and cysteine has been substituted for the aspartic
acid at position ~~84~~⁸³)

<400> 41

Lys Leu Phe Cys Asn Val Asn Cys Val Cys Asn Phe Ala Ser Arg Asn
1 5 10 15
Asp Tyr Ser

<210> 42

<211> 27

<212> PRT

<213> Artificial Sequence

<220>

<223> P2 (amino acids ~~68-95~~^{68 94} of SEQ ID NO:10; lysine has
been substituted for the leucine residue at
position ~~68~~ of the full-length Tumstatin molecule,
and aspartic acid has been substituted for the
cysteine residues at positions ~~80~~ and ~~85~~^{79 85})

<400> 42

Lys Gln Arg Phe Thr Thr Met Pro Phe Leu Phe Asp Asn Val Asn Asp
 1 5 10 15
 Val Asp Asn Phe Ala Ser Arg Asn Asp Tyr Ser
 20 25

<210> 43

<211> 27

<212> PRT

<213> Artificial Sequence

<220>

<223> Scrambled peptide SP1

<400> 43

Ala Asn Met Ser Arg Asn Val Phe Phe Asp Cys Thr Ser Phe Pro Val
 1 5 10 15
 Cys Gln Lys Phe Leu Asn Asp Thr Arg Asn Tyr
 20 25

<210> 44

<211> 27

<212> PRT

<213> Artificial Sequence

<220>

<223> Scrambled peptide SP2

<400> 44

Thr Phe Asn Cys Val Lys Asn Tyr Gln Arg Leu Asp Phe Thr Ser Arg
 1 5 10 15
 Phe Val Met Asp Ser Cys Ala Asn Phe Pro Asn
 20 25

<210> 45

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Generic peptide

<223> X at position 1 is a ^{any amino acid} ~~hydrogen or a peptidyl chain~~
~~of 1 to 17 amino acids~~

<223> X at position 2 is ^{Phe Lys} F or K

<223> X at position 5 is ^{Cys Ser Asp} C, S or D

<223> X at position 9 is ^{Asp Cys} D or C

<223> X at position 11 is ^{Cys Ser Asp} C, S or D

<223> X at position 14 is a ^{any amino acid} ~~hydrogen or a peptidyl chain~~
~~of 1 to 12 amino acids~~

<400> 45

Xaa Xaa Leu Phe Xaa Asn Val Asn Xaa Val Xaa Asn Phe Xaa
1 5 10

<210> 46

<211> 4

<212> PRT

<213> Artificial Sequence

<220>

<223> Generic peptide

<400> 46

Thr Thr Met Pro
1

<210> 47

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> Generic peptide

<400> 47

Phe Thr Thr Met Pro
1 5

<210> 48

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Generic peptide

<400> 48

Arg Phe Thr Thr Met Pro
1 5

<210> 49

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Generic peptide

<400> 49

Gln Arg Phe Thr Thr Met Pro
1 5

<210> 50

<211> 8

<212> PRT
<213> Artificial Sequence

<220>
<223> Generic peptide

<400> 50
Leu Gln Arg Phe Thr Thr Met Pro
1 5

<210> 51
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Generic peptide

<400> 51
Lys Gln Arg Phe Thr Thr Met Pro
1 5

<210> 52
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Generic peptide

<400> 52
Ala Ser Arg Asn
1

<210> 53
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Generic peptide

<400> 53
Ala Ser Arg Asn Asp
1 5

<210> 54
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Generic peptide

<400> 54

Ala Ser Arg Asn Asp Tyr
1 5

<210> 55

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Generic peptide

<400> 55

Ala Ser Arg Asn Asp Tyr Ser
1 5

<210> 56

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Generic peptide

<400> 56

Ala Ser Arg Asn Asp Tyr Ser Tyr
1 5

<210> 57

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Generic peptide

<400> 57

Ala Ser Arg Asn Asp Tyr Asp Tyr Trp
1 5

<210> 58

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Generic peptide

<400> 58

Ala Ser Arg Asn Asp Tyr Ser Tyr Trp Leu
1 5 10